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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/521,936	02/07/2006	Joseph M. Kaminski	0088567-027US0	6143

36257 7590 01/19/2011

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EXAMINER	
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ART UNIT	PAPER NUMBER
1633	

NOTIFICATION DATE	DELIVERY MODE
01/19/2011	ELECTRONIC

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BEFORE THE BOARD OF PATENT APPEALS
AND INTERFERENCES

Application Number: 10/521,936
Filing Date: February 07, 2006
Appellant(s): KAMINSKI, JOSEPH M.

Karen Lai
For Appellant

EXAMINER'S ANSWER

This is in response to the appeal brief filed September 3, 2010 appealing from the Office action mailed July 6, 2009.

(1) Real Party in Interest

The examiner has no comment on the statement, or lack of statement, identifying by name the real party in interest in the brief.

(2) Related Appeals and Interferences

The examiner is not aware of any related appeals, interferences, or judicial proceedings which will directly affect or be directly affected by or have a bearing on the Board's decision in the pending appeal.

(3) Status of Claims

The following is a list of claims that are rejected: Claims 1, 5-6, 15, 18, 20 and 23. Claims 2-4, 19, and 24-26 are pending but have been withdrawn from examination based on a species election.

It is noted that with respect to the restriction requirement, that upon review of the instant rejections and pending claims, the integration enzyme species election requirement set forth in the Requirement for Restriction in the Office Action mailed December 12, 2007 **is withdrawn**. Based on the current record per Elledge et al (U.S. Patent 6,828,093) disclosing that "the term "site-specific recombinase" refers to enzymes that recognize short DNA sequences that become the crossover regions during the recombination event and includes recombinases, transposases, and integrases." (col. 17, lines 16-19), each of the species in view of the art of record are obvious one over the other as presently claimed. At this time, the withdrawal of the election of species directed to the genus of integration enzyme species does not require any rejoinder of new claims nor new rejections over the pending claims.

(4) Status of Amendments After Final

The examiner has no comment on the appellant's statement of the status of amendments after final rejection contained in the brief.

(5) Summary of Claimed Subject Matter

The examiner has no comment on the summary of claimed subject matter contained in the brief.

(6) Grounds of Rejection to be Reviewed on Appeal

The examiner has no comment on the appellant's statement of the grounds of rejection to be reviewed on appeal. Every ground of rejection set forth in the Office action from which the appeal is taken (as modified by any advisory actions) is being maintained by the examiner except for the grounds of rejection (if any) listed under the subheading "WITHDRAWN REJECTIONS." New grounds of rejection (if any) are provided under the subheading "NEW GROUNDS OF REJECTION."

(7) Claims Appendix

The examiner has no comment on the copy of the appealed claims contained in the Appendix to the appellant's brief.

(8) Evidence Relied Upon

6,479,626	Kim et al	11-2002 (filed 3-1999)
6,828,093	Elledge et al	12-2004 (filed 7-1998)
2002/0116723	Grigliatti et al	8-2002 (filed 6-2001)

Handler et al. PNAS 95:7520-7525, 1998

Katz et al. Virology 217:178-190, 1996

McFarlane et al. Transgenic Res. 5(3):171-177, 1996; Abstract only

(9) Grounds of Rejection

The following ground(s) of rejection are applicable to the appealed claims:

As noted above in section (3), the restriction requirement for a specific species to an integration enzyme species as set forth in the Requirement for Restriction in the Office Action mailed December 12, 2007 **is withdrawn.** The rejections of record over the pending claims have not been modified and are maintained in light of the teaching of Elledge et al (U.S. Patent 6,828,093) disclosing that "the term "site-specific recombinase" refers to enzymes that recognize short DNA sequences that become the crossover regions during the recombination event and includes recombinases, transposases, and integrases." (col. 17, lines 16-19).

Claims 1, 5-6, 15, 18 and 20 are rejected under 35 U.S.C. 103(a) as being unpatentable over Handler et al (PNAS 95:7520-7525, 1998) in view of Kim et al (U.S. Patent 6,479,626), Katz et al (Virology 217:178-190, 1996), Elledge et al (U.S. Patent 6,828,093) and Grigliatti et al (U.S. 2002/0116723).

Determining the scope and contents of the prior art

Handler et al teach a composition comprising a first nucleic acid comprising a transgene flanked by two terminal repeats and a second nucleic acid encoding an integrating enzyme under the control of a promoter element. The first and second nucleic acids are separate plasmids (pgs 7520-7521, joining ¶, Plasmids; pg 7523, Figure 2A). The integrating enzyme is a transposase, more specifically from piggyBac. Given that the piggyBac transposase is on a separate plasmid from the first nucleic acid molecule, the transposase is considered to be "located outside the terminal repeats" of the first nucleic acid.

Handler et al do not teach the integrating enzyme to be a chimeric integrating enzyme. However, at the time of the invention, Kim et al disclosed recombinant DNA-binding proteins which include zinc finger and helix-loop-helix motifs (see abstract and introduction). The chimeric zinc finger proteins of the invention are composed of two or more DNA-binding domains, where at least one of the DNA binding domains is a zinc finger polypeptide. The second DNA binding domain can be a zinc finger binding domain, either the same domain or a heterologous domain. The second DNA binding domain can also be a heterologous host-specific

DNA binding domain, e.g., from a restriction enzyme; a nuclear hormone receptor; a homeodomain protein or a helix turn helix motif protein (col. 6, lines 28-45) and comprise a regulatory domain that has a DNA modifying activity such as found in integrases and recombinases (col. 10, lines 54-63). Expression of the chimeric proteins can be controlled by systems typified by the inducible tetracycline-regulated systems (col. 6, lines 62-64; col. 17, lines 44-49).

Neither Handler et al nor Kim et al disclose the host-specific DNA-binding domain to be fused to the N-terminus of the transposase. However, at the time of the invention, Katz et al taught a chimeric integrating enzyme, wherein the DNA-binding domain of LexA is fused to the catalytic domain of integrase, wherein the LexA DBD was present at the N-terminus of the fusion protein (pg 181, col. 1, ¶2).

Similarly, Grigliatti et al disclosed transposon-based transformation vectors comprising the use of transposase, e.g. piggyBac [0229], wherein the transposon vector comprises terminal repeats, and wherein the transposase gene and heterologous protein expression cassette are within or outside the transposon termini [0026]. While the transposase is expressed, the enzyme directs the entry of the transposon into the genomic DNA. Transposase expression may be modulated to regulate the movement of the transposon, thereby controlling transposon copy number [0025].

Resolving the level of ordinary skill in the pertinent art, and Ascertaining the differences between the prior art and the claims at issue

People of the ordinary skill in the art will be highly educated individuals such as doctors, scientists, or engineers, possessing advanced degrees, including M.D.'s and Ph.D.'s. Thus, these people most likely will be knowledgeable and well-read in the relevant literature and have the practical experience in molecular biology, recombination cloning, and the creation of transgenic cells and organisms using transposable elements. Therefore, the level of ordinary skill in this art is high.

At the time of the invention, Elledge et al disclosed that site-specific recombinases refers to enzymes that recognize short DNA sequences that become the cross-over regions during the recombination event and includes recombinases, transposases and integrases (col. 17, lines 15-

19). Thus, at the time of the invention, piggyBac transposase was an art-recognized species within the genus of site-specific recombination enzymes comprising transposases, integrases and recombinases.

Considering objective evidence present in the application indicating obviousness or nonobviousness.

It would have been obvious to one of ordinary skill in the art to modify the piggyBac transposase to comprise a heterologous host-specific DNA-binding domain with a reasonable expectation of success because the prior art (e.g. Katz et al) had successfully demonstrated that the catalytic recombination activity of site-specific recombination enzymes were functional when operably linked to a heterologous DNA-binding domain. An artisan would be motivated to modify the piggyBac transposase to comprise a heterologous host-specific DNA-binding domain because Kim et al disclose that the heterologous design allows one to increase the affinity of the DNA binding polypeptide for its target DNA (see introduction) and Katz et al teach that the integrating enzymatic activity may be influenced or enhanced by fusion to a heterologous DNA-binding domain so as to enhance or target integration at a desired target site (pg 179, col. 1, ¶2-3). Katz et al suggest that such a chimeric fusion strategy may be useful for targeting or enhancing integration of a nucleic acid vector in vivo (pg 189, col. 1, ¶1; col. 2).

It also would have been obvious to substitute the promoter operably linked to the piggyBac transposase with a tetracycline-inducible promoter with a reasonable expectation of success because the simple substitution of one known element for another would have yielded predictable results to one of ordinary skill in the art at the time of the invention. An artisan would be motivated to substitute the promoter operably linked to the piggyBac transposase with a tetracycline-inducible promoter because the tetracycline-inducible system has long been recognized to provide the artisan with significant transcriptional control over the timing and expression level of the desired gene expression product.

It also would have been obvious to one of ordinary skill in the art to combine the first nucleic acid comprising a transgene flanked by two terminal repeats and the second nucleic acid encoding an integrating enzyme under the control of a promoter element in the same nucleic acid molecule with a reasonable expectation of success because "a person of ordinary skill has good

reason to pursue the known options within his or her technical grasp. If this leads to the anticipate success, it is likely that product not of innovation but of ordinary skill and common sense.", and all the claimed elements were known in the prior art and one skilled in the art could have combined the elements as claimed by known methods with no change in their respective functions, and the combination would have yielded predictable results to one of ordinary skill in the art at the time of the invention. There are only two formal possible combinations between the first and second nucleic acid molecules, either they are within the same nucleic acid molecule or are in separate nucleic acid molecule. An artisan would be motivated to combine the first nucleic acid comprising a transgene flanked by two terminal repeats and the second nucleic acid encoding an integrating enzyme under the control of a promoter element in the same nucleic acid molecule because it is but one of two possible choices and the art recognizes that both permutations will achieve transposition of the desired heterologous nucleic acid.

Grigliatti et al do not disclose that the transposase would be positioned outside the terminal repeats of the transposon. However, it also would have been obvious to one of ordinary skill in the art to try positioning the transposase outside the terminal repeats of the transposon when the first nucleic acid comprising a transgene flanked by two terminal repeats and the second nucleic acid encoding an integrating enzyme under the control of a promoter element are the same nucleic acid molecule because "a person of ordinary skill has good reason to pursue the known options within his or her technical grasp. If this leads to the anticipate success, it is likely that product not of innovation but of ordinary skill and common sense." There are only two possible placements of the nucleic acid molecule encoding the transposase: either within or outside the terminal repeats. Given the art-recognized mechanism of transposition, those nucleic acids within the terminal repeats will be integrated into the host cell genome; whereas, those nucleic acids outside the terminal repeats will not integrate. An artisan would be motivated to try positioning the transposase outside the terminal repeats of the transposon when the first nucleic acid comprising a transgene flanked by two terminal repeats and the second nucleic acid encoding an integrating enzyme under the control of a promoter element are the same nucleic acid molecule so as to establish stable integration of the desired transgene.

Thus, absent evidence to the contrary, the invention as a whole is prima facie obvious.

Claim 23 is rejected under 35 U.S.C. 103(a) as being unpatentable over Handler et al (PNAS 95:7520-7525, 1998) in view of Kim et al (U.S. Patent 6,479,626), Katz et al (Virology 217:178-190, 1996), Elledge et al (U.S. Patent 6,828,093) and Grigliatti et al (U.S. 2002/0116723), as applied to claims 1, 5-6, 15, 18 and 20 above, and in further view of McFarlane et al (Transgenic Res. 5(3):171-177, 1996; Abstract only).

Determining the scope and contents of the prior art

Neither Handler et al, Kim et al, Katz et al, Elledge et al nor Grigliatti et al disclose the nucleic acid composition to further comprise a homologous sequence that is homologous to the host DNA. However, at the time of the invention, McFarlane et al taught the inclusion of a nucleic acid sequence having 5 base pairs that were homologous to the host DNA. McFarlane suggest that this feature was likely to have been factorial in the insertion event, and propose a model depicting a mechanism by which precise integration may occur.

Resolving the level of ordinary skill in the pertinent art.

People of the ordinary skill in the art will be highly educated individuals such as doctors, scientists, or engineers, possessing advanced degrees, including M.D.'s and Ph.D.'s. Thus, these people most likely will be knowledgeable and well-read in the relevant literature and have the practical experience in molecular biology, recombination cloning, and the creation of transgenic cells and organisms using transposable elements. Therefore, the level of ordinary skill in this art is high.

The Examiner notes that the claim does not specify either the minimal length or the location of the sequence that is homologous to the host DNA, and at present a single nucleotide anywhere in the nucleic acid(s) would reasonably fulfill the instantly claimed limitation.

Considering objective evidence present in the application indicating obviousness or nonobviousness.

It would have been obvious to one of ordinary skill in the art to combine a homologous sequence that is homologous to the host DNA with a nucleic acid composition comprising a transgene flanked by two terminal repeats and a nucleic acid encoding an integrating enzyme

under the control of a promoter element with a reasonable chance of success because all the claimed elements were known in the prior art and one skilled in the art could have combined the elements as claimed by known methods with no change in their respective functions, and the combination would have yielded predictable results to one of ordinary skill in the art at the time of the invention. An artisan would be motivated to combine a homologous sequence that is homologous to the host DNA with a nucleic acid composition comprising a transgene flanked by two terminal repeats and a nucleic acid encoding an integrating enzyme under the control of a promoter element because at the time of the invention, those of ordinary skill in the art had long recognized that the inclusion of nucleic acid sequences homologous to the host DNA would significantly improve the likelihood that the transformation vector would integrate at a desired location in the host genome. Such has been standard practice for the generation of transgenic mice.

Thus, the invention as a whole is prima facie obvious.

(10) Response to Argument

Claims 1, 5-6, 15, 18 and 20 are rejected under 35 U.S.C. 103(a) as being unpatentable over Handler et al (PNAS 95:7520-7525, 1998) in view of Kim et al (U.S. Patent 6,479,626), Katz et al (Virology 217:178-190, 1996), Elledge et al (U.S. Patent 6,828,093) and Grigliatti et al (U.S. 2002/0116723).

Response to Arguments

Appellant argues that the Examiner has reversed his own previous determination that transposases, recombinases and integrases are not obvious variants of each other to illustrate the obviousness of claims directed to transposases. The Examiner required a species election between transposases, integrases and recombinases "due to their mutually exclusive characteristics," holding that "the species are not obvious variant of each another based on the current record" and that "the prior art applicable to one species would not likely be applicable to another species. In particular, in the Requirement for Restriction, the Examiner stated "Prior to the invention, the art had long-recognized that each integrating enzyme possesses its own special technical feature because each enzyme recognizes a distinctly different nucleic acid sequence,

thereby generating site-specificity for integration and/or excision of the nucleic acid." Appellant understood this to be a final determination, and fully complied with the species election in good faith, neither traversing nor petitioning the requirement. Appellant reasonably understood that the Examiner had determined these to be "patentably distinct species" and would therefore not raise prior art directed to integrases and recombinases against claims directed to transposases. It was an error for the Examiner to have reversed the determination in order to expand the universe of prior art available to establish obviousness.

Appellant's argument(s) has been fully considered, but is not persuasive. The integration enzyme species election requirement set forth in the Requirement for Restriction in the Office Action mailed December 12, 2007 has been withdrawn based on the current record per Elledge et al (U.S. Patent 6,828,093) disclosing that "the term "site-specific recombinase" refers to enzymes that recognize short DNA sequences that become the crossover regions during the recombination event and includes recombinases, transposases, and integrases." (col. 17, lines 16-19) Upon a search and examination of the claims, the Examiner found that those of ordinary skill in the art consider transposases, recombinases and integrases to be species within the same genus of site-specific recombination enzymes. Elledge et al disclosed that site-specific recombinases refers to enzymes that recognize short DNA sequences that become the cross-over regions during the recombination event and includes recombinases, transposases and integrases (col. 17, lines 15-19). Elledge et al teach that those of ordinary skill in the art recognize transposases, integrases, and recombinases to be enzymes that recognize short DNA sequences that become the crossover regions during the recombination event, thereby integrating a first DNA molecule with another DNA molecule. Regardless of the mechanism, the same functional result is achieved, namely site-specific integration. Thus, at the time of the invention, the enzymatic recombination property of piggyBac transposase was an art-recognized species within the genus of site-specific recombination enzymes comprising transposases, integrases and recombinases.

The Examiner must determine what is "analogous prior art" for the purpose of analyzing the obviousness of the subject matter at issue. **>"Under the correct analysis, any need or problem known in the field of endeavor at the time of the invention and addressed by the patent [or application at issue] can provide a reason for combining the elements in the manner claimed. " KSR International Co. v. Teleflex Inc., 82 USPQ2d 1385, 1397 (2007). Thus a reference in a

field different from that of Appellant's endeavor may be reasonably pertinent if it is one which, because of the matter with which it deals, logically would have commended itself to an inventor's attention in considering his or her invention as a whole.<

It would have been obvious to one of ordinary skill in the art to modify the piggyBac transposase to comprise a heterologous host-specific DNA-binding domain with a reasonable expectation of success because the prior art (e.g. Katz et al) had successfully demonstrated that the catalytic recombination activity of site-specific recombination enzymes were functional when operably linked to a heterologous DNA-binding domain. An artisan would be motivated to modify the piggyBac transposase to comprise a heterologous host-specific DNA-binding domain because Kim et al disclose that the heterologous design allows one to increase the affinity of the DNA binding polypeptide for its target DNA (see introduction) and Katz et al teach that the integrating enzymatic activity may be influenced or enhanced by fusion to a heterologous DNA-binding domain so as to enhance or target integration at a desired target site (pg 179, col. 1, ¶2-3). Katz et al suggest that such a chimeric fusion strategy may be useful for targeting or enhancing integration of a nucleic acid vector in vivo (pg 189, col. 1, ¶1; col. 2).

Appellant argues that the Examiner made in the Final Office Action dated December 18, 2008, in which the Examiner stated that "[n]either Handler et al, Kim et al nor Katz et al teach that the genus of integrases and recombinases embraces transposases" and relied on the disclosure of Elledge, a U.S. patent, to teach that site-specific recombinases include recombinases, transposases and integrases. This distinction is important: the Examiner relied on the disclosure of Elledge, which defines site-specific recombinases (not site-specific recombination enzymes generally) to assert that art directed to recombinases and integrases could be used in an obviousness rejection for claims directed to piggyBac transposase. Thus, the reliance on Elledge for obviousness no longer appears proper in view of the Examiner's current arguments.

Appellant's argument(s) has been fully considered, but is not persuasive. The focus when making a determination of obviousness should be on what a person of ordinary skill in the pertinent art would have known at the time of the invention, and on what such a person would have reasonably expected to have been able to do in view of that knowledge. This is so

regardless of whether the source of that knowledge and ability was documentary prior art, general knowledge in the art, or common sense. M.P.E.P. §2141.

The person of ordinary skill in the art is a hypothetical person who is presumed to have known the relevant art at the time of the invention. Factors that may be considered in determining the level of ordinary skill in the art may include: (1) "type of problems encountered in the art;" (2) "prior art solutions to those problems;" (3) "rapidity with which innovations are made;" (4) "sophistication of the technology; and" (5) "educational level of active workers in the field. In a given case, every factor may not be present, and one or more factors may predominate." In re GPAC, 57 F.3d 1573, 1579, 35 USPQ2d 1116, 1121 (Fed. Cir. 1995); Custom Accessories, Inc. v. Jeffrey-Allan Industries, Inc., 807 F.2d 955, 962, 1 USPQ2d 1196, 1201 (Fed. Cir. 1986); Environmental Designs, Ltd. V. Union Oil Co., 713 F.2d 693, 696, 218 USPQ 865, 868 (Fed. Cir. 1983).

Appellant appears to have exercised a narrow interpretation of Elledge et al, who disclosed that site-specific recombinases refers to enzymes that recognize short DNA sequences that become the cross-over regions during the recombination event and includes recombinases, transposases and integrases (col. 17, lines 15-19). Given Elledge's definition, the Examiner interprets the Elledge disclosure to support that art directed to recombinases and integrases could be used in an obviousness rejection for claims directed to [piggyBac] transposase, and thus reliance on Elledge et al on what a person of ordinary skill in the pertinent art would have known at the time of the invention, and on what such a person would have reasonably expected to have been able to do in view of that knowledge, for making a determination of obviousness is proper.

Appellant argues that Elledge incorrectly defines the term "site-specific recombinase." At best, Elledge was acting as his own lexicographer in defining this term for the purposes of describing the claimed invention. However, this is not a reflection of what the Examiner himself correctly described as generally understood in the art, namely, that these enzymes are not interchangeable or obvious variants of each other.

Appellant's argument(s) has been fully considered, but is not persuasive. Elledge et al disclosed that site-specific recombinases refers to enzymes that recognize short DNA sequences that become the cross-over regions during the recombination event and includes recombinases,

transposases and integrases (col. 17, lines 15-19). The instant specification discloses that the purpose of the invention is for site-selective integration of nucleic acid molecules, achieved via fusion polypeptide comprising a DNA binding domain and any enzyme with integrating capabilities, including but not limited to transposases, integrases, and recombinases (pg 4, lines 2-4; pg 9, [51]). Thus, it appears that Appellant also recognizes transposases, integrases, and recombinases to be enzymes that recognize short DNA sequences that become the crossover regions during the recombination event, thereby integrating a first DNA molecule with another DNA molecule.

Those of ordinary skill in the art recognize transposases, integrases, and recombinases to be enzymes that recognize short DNA sequences that become the crossover regions during the recombination event, thereby integrating a first DNA molecule with another DNA molecule. Regardless of the mechanism, the same functional result is achieved, namely site-specific integration. Thus, at the time of the invention, piggyBac transposase was an art-recognized species within the genus of site-specific recombination enzymes comprising transposases, integrases and recombinases.

Appellant argues that Elledge published as U.S. Patent No. 6,828,093 on December 7, 2004, which post-dates the priority date of the instant application (July 24, 2002). Accordingly, the Examiner has improperly applied Elledge as a critical reference to reject the claims under 35 U.S.C. §103.

Appellant's argument(s) has been fully considered, but is not persuasive. Appellant is respectfully reminded that the Elledge et al application was originally filed July 24, 1998. Thus, reliance on Elledge et al on what a person of ordinary skill in the pertinent art would have known at the time of the invention (2002, four years after the filing of Elledge et al), and on what such a person would have reasonably expected to have been able to do in view of that knowledge, for making a determination of obviousness is proper.

Appellant argues that it is clear from Coates that "site-specific recombinases" are distinct from viral integrases and transposases and do not encompass them. In addition, when read in its entirety, it is clear from Coates that a person of ordinary skill in the art would consider

transposases, recombinases and integrases to be distinctly different in both evolutionary and mechanistic terms. The Examiner asserts that the same functional result is achieved, namely site-specific integration. However, the Examiner fails to take into account that the different mechanisms and specificity of integration among transposases, recombinases and integrases would not make it obvious to the skilled artisan to substitute one type of enzyme for another, or to apply the teachings of one type of enzyme to either of the other types.

Appellant's argument(s) has been fully considered, but is not persuasive. Elledge et al disclosed that site-specific recombinases refers to enzymes that recognize short DNA sequences that become the cross-over regions during the recombination event and includes recombinases, transposases and integrases (col. 17, lines 15-19). Similarly, Coates et al (2005; *of record in IDS) to which Appellant refers, also teaches that integrases, transposases and recombinases share the same functional property of catalyzing the insertion of foreign DNA into a target nucleic acid (pg 407, col. 2, "tools of the trade"). Thus, those of ordinary skill in the art recognize transposases, integrases, and recombinases to be enzymes that recognize short DNA sequences that become the crossover regions during the recombination event, thereby integrating a first DNA molecule with another DNA molecule. Regardless of the mechanism, the same functional result is achieved, namely site-specific integration. Thus, the different mechanisms among transposases, recombinases and integrases would make it obvious to one of ordinary skill in the art to substitute one type of enzyme for another, and to apply the teachings of one type of enzyme to either of the other types.

Appellant argues that the claims relate to a composition containing a single nucleic acid construct that includes (i) a transgene, flanked by piggyBac transposon-derived terminal repeats, to be integrated into a target host genome for non-transient expression in the host, and (ii) a nucleic acid sequence that encodes a chimeric integrating enzyme that catalyzes integration of the transgene into the target hast genome. Handler is directed to a two-vector system.

Appellant's argument(s) has been fully considered, but is not persuasive. Appellant's specification discloses that "As used in the specification and the appended claims, the singular forms "a," "an" and "the" include plural referents unless the context clearly dictates otherwise."

[34]. Thus, the instant claims reasonably embrace plural nucleic acid constructs, not just a single construct. Claim 1 does not recite "a single nucleic acid construct".

Appellant argues that the art directed to integrases and recombinases (Kim, Katz) is not applicable to piggyBac transposase in view of the species election. Elledge has already been addressed in terms of its incorrect definition of "site-specific recombinase." The remaining combination of references, Handler and Grigliatti, do not reach or suggest the claimed subject matter of a single nucleic acid construct containing a transgene flanked by piggyBac transposon-derived terminal repeats and a region that encodes a chimeric integrating having a zinc-finger-derived DNA binding domain and an enzymatic integrating domain derived from piggyBac transposase. Accordingly, Appellant asserts that the claims are not obvious over the relevant combination of references.

Appellant's argument(s) has been fully considered, but is not persuasive. In response to Appellant's argument that art directed to integrases and recombinases is nonanalogous art, it has been held that a prior art reference must either be in the field of Appellant's endeavor or, if not, then be reasonably pertinent to the particular problem with which the Appellant was concerned, in order to be relied upon as a basis for rejection of the claimed invention. See In re Oetiker, 977 F.2d 1443, 24 USPQ2d 1443 (Fed. Cir. 1992). In this case, Kim et al is considered analogous prior art for disclosing chimeric DNA-binding domain proteins comprising host-specific DNA binding domains (c15; col. 6, lines 28-45), wherein the expression of the chimeric DNA-binding domain proteins is controlled by an inducible promoter, i.e. tetracycline-regulated system (c6; col. 6, lines 62-64; col. 17, lines 44-49). Thus, at the time of the instantly asserted invention, those of ordinary skill in the art were aware of the ability to express chimeric DNA-binding proteins via the use of an inducible promoter.

Similarly, Katz et al is considered analogous prior art for teaching a chimeric integrating enzyme, wherein the DNA-binding domain of LexA is fused to the catalytic domain of integrase, and wherein the LexA DBD was present at the N-terminus of the fusion protein (pg 181, col. 1, ¶2). Thus, at the time of the instantly asserted invention, those of ordinary skill in the art were aware of chimeric proteins comprising a DNA-binding and a heterologous recombination

enzymatic activity to catalyze the insertion of a first DNA molecule into a second DNA molecule.

Elledge et al disclosed that site-specific recombinases refers to enzymes that recognize short DNA sequences that become the cross-over regions during the recombination event and includes recombinases, transposases and integrases (col. 17, lines 15-19). Thus, those of ordinary skill in the art recognize transposases, integrases, and recombinases to be enzymes that recognize short DNA sequences that become the crossover regions during the recombination event, thereby integrating a first DNA molecule with another DNA molecule. Regardless of the mechanism, the same functional result is achieved, namely site-specific integration.

Thus, it is the Examiner's position that both Kim et al and Katz et al may be reasonably pertinent to the instantly asserted invention because of the matter with which it deals, logically would have commended itself to an inventor's attention in considering his or her invention as a whole. See MPEP §2141.01(a).

(11) Related Proceeding(s) Appendix

No decision rendered by a court or the Board is identified by the examiner in the Related Appeals and Interferences section of this examiner's answer.

For the above reasons, it is believed that the rejections should be sustained.

Respectfully submitted,

/Kevin K. Hill/

Primary Examiner, Art Unit 1633

Conferees:

/Joseph T. Woitach/

Supervisory Patent Examiner, Art Unit 1633

/Kathleen Kerr Bragdon/

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